PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference KXC/PG4890	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/11813	International filing date *(day/month/year)* 22.10.2003	Priority date *(day/month/year)* 24.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D417/04		
Applicant GLAXO GROUP LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the opinion
   II ☐ Priority
   III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   IV ☐ Lack of unity of invention
   V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   VI ☐ Certain documents cited
   VII ☐ Certain defects in the international application
   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05.05.2004	09.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Seitner, I Telephone No. +31 70 340-2389

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11813

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-105 as originally filed

Claims, Numbers

1-23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 13-15 (with respect to industrial applicability)

   because:

   ☒ the said international application, or the said claims Nos. 13-15 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-23
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-23
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-12,16-23
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 13-15 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 01/85720 A (SMITHKLINE BEECHAM CORP ;CARR THOMAS (US); DHANAK DASHYANT (US)) 15 November 2001 (2001-11-15)

D2: WO 00/09543 A (BOEHRINGER INGELHEIM CA LTD ;GOUDREAU NATHALIE (CA); GHIRO ELISE () 24 February 2000 (2000-02-24)

D3: WO 99/54299 A (ABBOTT LAB) 28 October 1999 (1999-10-28)

D4: JOURNAL OF HETEROCYCLIC CHEMISTRY 1989, 26(4), 1023-1027

V.1. Novelty:

Document D1 discloses compounds (see examples 1-147; claims 2, 4) for the treatment of hepatitis C which differ in that the substituent corresponding to G represents C(=O)D, whereas in the present application G represents alkyl which cannot be substituted by oxo.

Document D4 discloses compounds (see examples 5, 8, and 10) which fall within the scope of the general formula (I) of claim 16 which is directed to their use as medicaments. The compounds of D4 have only been disclosed as chemical intermediates and no biological activity has been associated with said compounds.

Therefore, the subject-matter of claims 1-23 is novel over the prior art (Article 33(2) PCT).

V.2. Inventive Step:

Document D1, which is considered to represent the most relevant state of the art, discloses HCV inhibitors from which the subject-matter of present claim 1 differs in that the substituent G represents hydrogen or alkyl, whereas in D1 the pyrrole ring has to be substituted by C(=O)D in the 4-position.

The problem to be solved may therefore be regarded as the provision of further compounds for the treatment of viral infections.

Document D3 discloses a very general formula of compounds for the treatment of viral infections (see claims 1, 33-56) and especially influenza, which differ from the subject matter of the present application in that the group substituting the nitrogen atom of the pyrrolidine ring cannot be C(=O)D and the examples disclosed in D3 do not comprise a substituent corresponding to the present substituent J.

In view of the teaching of the prior art, the skilled person would not have had a clear incentive to combine the documents D1 and D3 and moreover, to focus on the 4-position of the pyrrolidine ring and to modify said position according to the present formula (I).

Therefore, the subject-matter of claims 1-23 is considered as involving an inventive step in the sense of Article 33(3) PCT.

V.3. Industrial Applicability:

The present application relates to compounds which are useful for the treatment of viral infections and the subject matter of claims 1-12,16-23 is therefore considered as industrially applicable (Article 33(4) PCT).

For the assessment of the present claims 13-15 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known com-

pound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.